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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/546,132	12/12/2005	Rulin Fan	EISN-009US	9915
959 7590 11/02/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER ISSAC, ROY P	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 11/02/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/546,132

Applicant(s)

FAN, RULIN

Examiner

Roy P. Issac

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 120-123, 125-128, 130-133 and 135-138 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 120-123, 125-128, 130-133 and 135-138 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to Applicant's amendment/ remarks/ response filed 8/20/07, wherein claim 124, 129, 134 and 139 have been cancelled. Claims 120-123, 125-128, 130-133 and 135-138 are currently pending and are examined on the merits herein.

Rejections Withdrawn

In view of the cancellation of claims 124, 129, 134 and 139, all rejections made with respect to claims 124, 129, 134 and 139 in the previous office action are withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

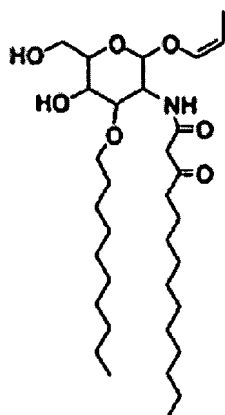
Claims 120-123, 125-128, 130-133 and 135-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossignol et. al. (U.S. Patent No. 6,184,366; Of Record).

Rossignol discloses the synthesis of liposaccharides with strong structural similarity to compounds of the instant application. The compounds of the instant

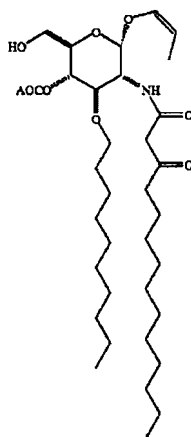
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application and compounds of the '366 patent are directed to the treatment of endotoxemia. (Abstract). The claimed compounds of the instant application are directed to the synthesis of liposaccharides used for the synthesis of lipodisaccharides. Rossignol discloses a synthetic route for the synthesis of liposaccharides. (Column 13-15). The synthetic strategy includes the use of cyclic acetal protecting groups for 6 and 4 position hydroxyl groups, allyl protecting group for hydroxyl and phosphate groups, as well as carbonate group for hydroxyl group. (Column 13-15). The trichloroacetonitrile protecting group, the TBS protecting group are also disclosed. (Column 19-20).

Compound of claim 125



Similar compound disclosed in the '366 patent

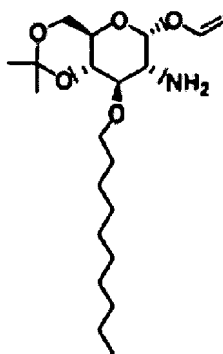


The only differences between these two compounds is the presence of the allyl carbonate protecting group in the '366 patent, which is removed in the final step of the synthesis. (Column 53-54, Synthetic scheme), and that claim 125 is directed to a racemic compound. Compounds of claim 126, 128, 135, 136 and 138 only differ from the illustrated compound of the '366 patent in the presence and absence of commonly used protecting groups for hydroxyl groups in carbohydrate chemistry.

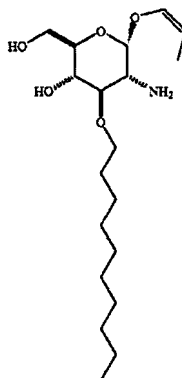
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Compounds of claims 120-123, and 130-134 of the instant application differs from the above illustrated compound of the '366 patent in the presence of the cis-11-octadecanoyl side chain instead of the dioxotetradecyl side chain. The '366 patent further discloses the synthesis of lipodisaccharide with cis-11-octadecenoyl chloride. (Column 49-50).

Compounds of claim 137:



Compound of the '366 patent (Column 39):



The only difference between compound 137 and the above illustrated compound of the '366 patent is the presence of a cyclic acetal protecting group for the two hydroxyl groups the sugar moiety. Claim 127 is directed to the racemic form of the compound of claim 137. The '366 patent further discloses the use of cyclic acetal groups to protect the same hydroxyl groups of the sugar moiety. (For example, synthetic scheme Column 13-14; Column 37-38).

The '366 patent does not expressly disclose the particular compounds of the instant application.

It would have been obvious to one of ordinary skill in the art to synthesize compounds of instant application because the '366 patent discloses compounds with the same core structure as the instant application and discloses the use of the same protecting groups in the synthesis of compounds of similar structure. The synthesis of similar compounds, with the expectation that similar compounds would result in similar properties, would require the protection and deprotection of hydroxyl groups with different types of protecting groups. Such manipulation of synthetic strategy is considered well within the basic skill of one of ordinary skill in the art and the particular methods of protecting and deprotecting groups are disclosed in the '366 patent. Furthermore, the '366 patent broadly discloses a genus of compounds of Formula I which would give reason for one of ordinary skill in the art to pursue basic changes in the synthetic strategies including the use of different types of protecting groups to synthesize a large number of the disclosed genus. All the claimed steps herein are known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *Deuel*, 51 F.3d at 1558, 34 USPQ2d at

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1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. *Id.* Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species. In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; *In re Wilder*, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

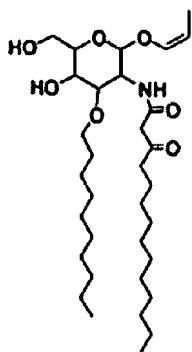
Thus, one of ordinary skill in the art would have reasonably expected compounds with similar structure, with only difference in protecting groups, would have resulted in compounds useful for the synthesis of many of the structurally similar compounds encompassed by Formula I for the treatment of endotoxemia with substantially similar or better properties.

Thus, the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

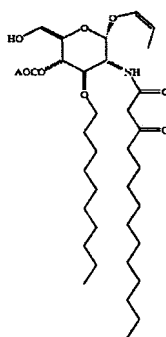
Response to Arguments

Applicant's arguments filed 8/20/07 have been fully considered but they are not persuasive. Applicants further argue that one of ordinary skill in the art would have had no reason to modify the known compounds of Christ in the particular manner described in the present invention. However, as noted above, the '366 patent discloses a genus of compounds encompassed by the Formula I, the synthesis of a substantial number of which would require the use of different protecting groups for the several hydroxyl groups of the sugar moiety. Such need would have given one of ordinary skill in the art reason to pursue multiple protecting groups for and their deprotection to synthesize many of the species encompassed by the genus.

Compound of claim 125



Similar compound disclosed in the '366 patent



As noted above, the only differences between the two compounds shown above is the presence of a protecting group AOC for the hydroxyl. The method for removing the protecting group is also disclosed in the '366 patent. (See scheme Columns 21-22). The '366 patent also discloses a genus of compounds encompassed by the general formula I. (Columns 4-5). The synthesis of similar compounds, with the expectation

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that similar compounds would result in similar properties, would require the protection and deprotection of hydroxyl groups with different types of protecting groups. In fact, the synthesis scheme herein disclosed by the applicant converts the above compound to its AOC protected derivative before coupling with the second sugar moiety. (See figure below excerpted from Page 92, Scheme 1)

As noted above, if the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species. In fact, similar properties may normally be presumed when compounds are very close in structure. *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. *Dillon*, 919 F.2d at 697-98, 16 USPQ2d at 1905; *In re Wilder*, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). The methodology for protection and deprotection using commonly used protecting groups such as AOC-, (AllylO)₂OP-, Troc are well known by one of ordinary skilled in the art and are exemplified in the '366 patent. Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared

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by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious.

Applicants argue that the present invention allows for the synthesis of the final product without the use of Troc intermediate while Christ et. al. requires the activation of the amine group with Troc before attachment of the long-chain alkanoyl groups. However, the claims herein are directed to particular compounds. The method of preparation using them is considered as intended use of the compounds. Note that it is well settled that "intended use" of a composition or product will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as the instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161. Furthermore, the intended uses are not limitations of the claims herein. Applicants further argue that Christ does not suggest or disclose the direct attachment of the long chain alkanoyl group without the use of the Troc group. (See page 12 of the argument, Scheme 2). However, Christ discloses the same protecting group, (AllylO)₂OP- for the same position as disclosed in Scheme 2 of applicants arguments. (See Columns 21-22). While the applicant might have saved the step of deprotecting Troc group before coupling the two saccharide groups, applicant compensated for that by having to deprotect and protect other positions of the saccharide hydroxyls. This is a distinction without a difference. It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a)-(g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in

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results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex Parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing". *In re Lohr*, 137 USPQ 548 (CCPA 1963), *In re Linder*, 173 USPQ 356 (CCPA 1972). The compounds herein represent the same underlying compounds as the '366 patent which substantially uses the same protecting groups but with changes in the position and the sequence of addition of the saccharide units and the alkyl chain without any surprising results. The rejection under section 103 is still deemed proper and is adhered to.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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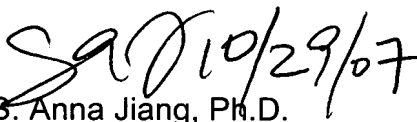
the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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